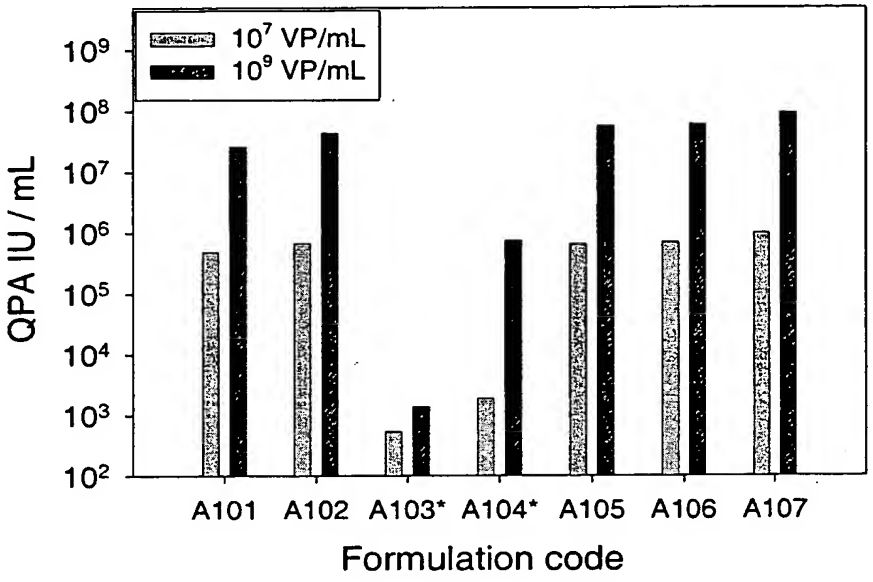
Figure 1. Effect of one freeze/thaw cycle on the stability of Ad5gag in candidate formulations



*QPA assays of these two formulations showed either little infection or wide margin of error.

Variability of assay ~ 0.15 logs.

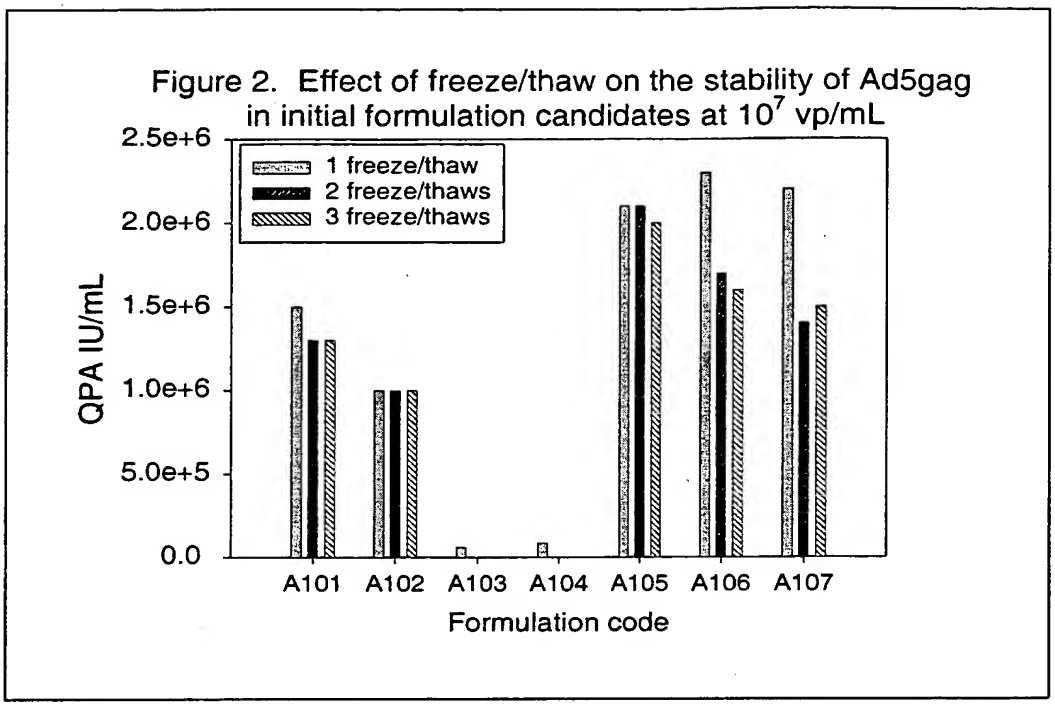


Figure 2. Effect of freeze/thaw on the stability of Ad5gag in initial formulation candidates at 10^7 vp/mL
2.5e+6
2.0e+6
1.5e+6
1.0e+6
5.0e+5
0.0
QPA IU/mL
1 freeze/thaw
2 freeze/thaws
3 freeze/thaws
A101
A102
A103
A104
A105
A106
A107
Formulation code

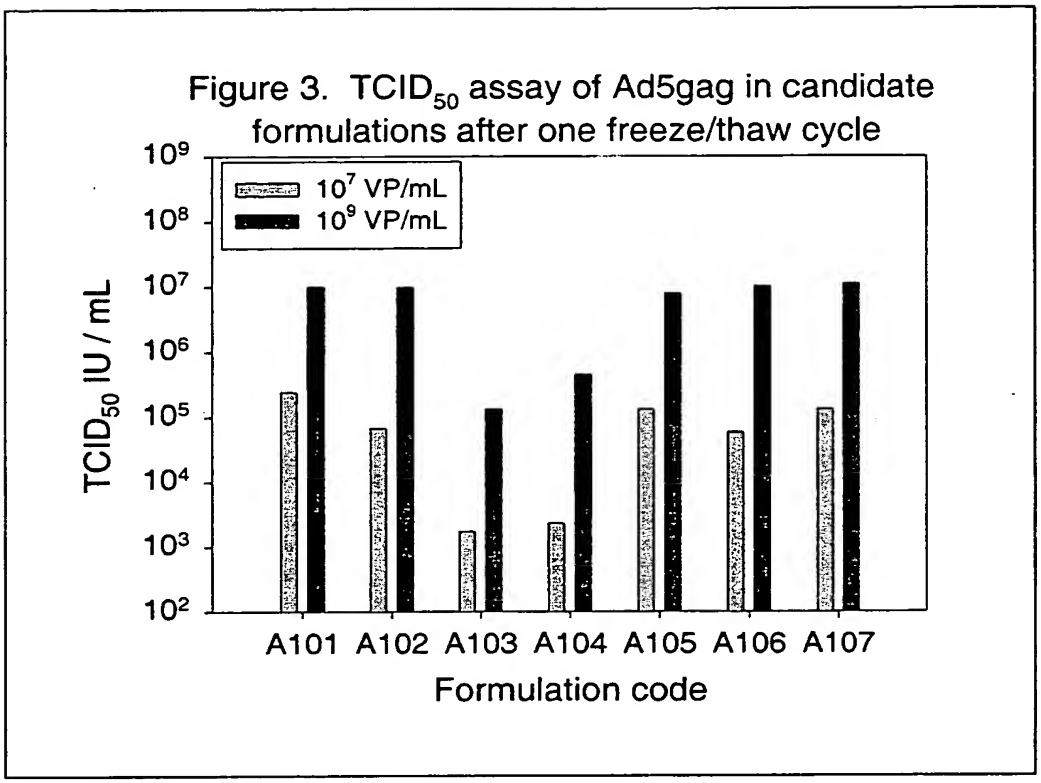


Figure 3. TCID50 assay of Ad5gag in candidate formulations after one freeze/thaw cycle
10^9 VP/mL
10^7 VP/mL
TCID50 IU / mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
A101 A102 A103 A104 A105 A106 A107
Formulation code

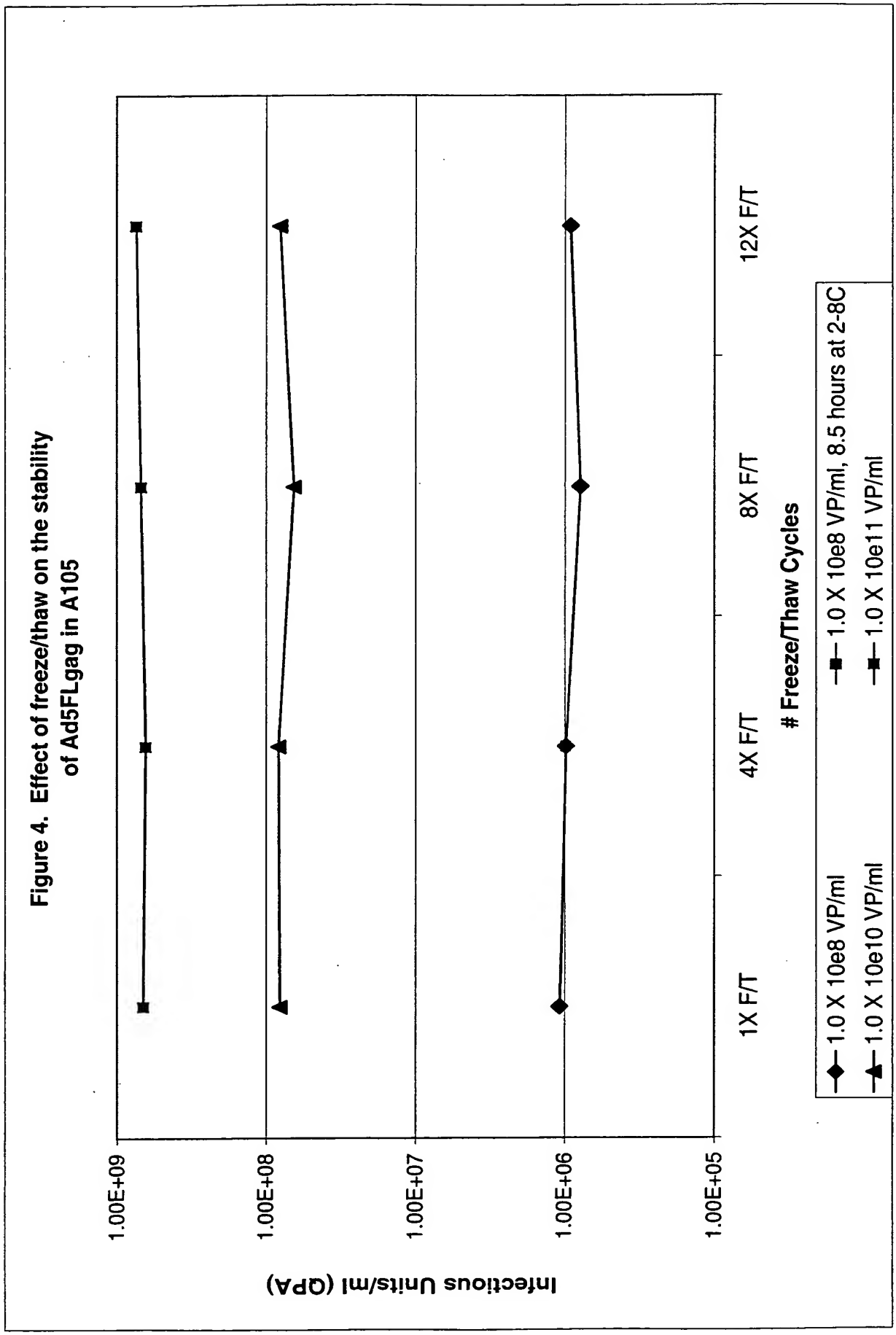


Figure 4. Effect of freeze/thaw on the stability of Ad5FLgag in A105
Infectious Units/ml (QPA)
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
1X F/T
4X F/T
8X F/T
12X F/T
Freeze/Thaw Cycles
1.0 X 10e8 VP/ml
1.0 X 10e8 VP/ml, 8.5 hours at 2-8C
1.0 X 10e10 VP/ml
1.0 X 10e11 VP/ml

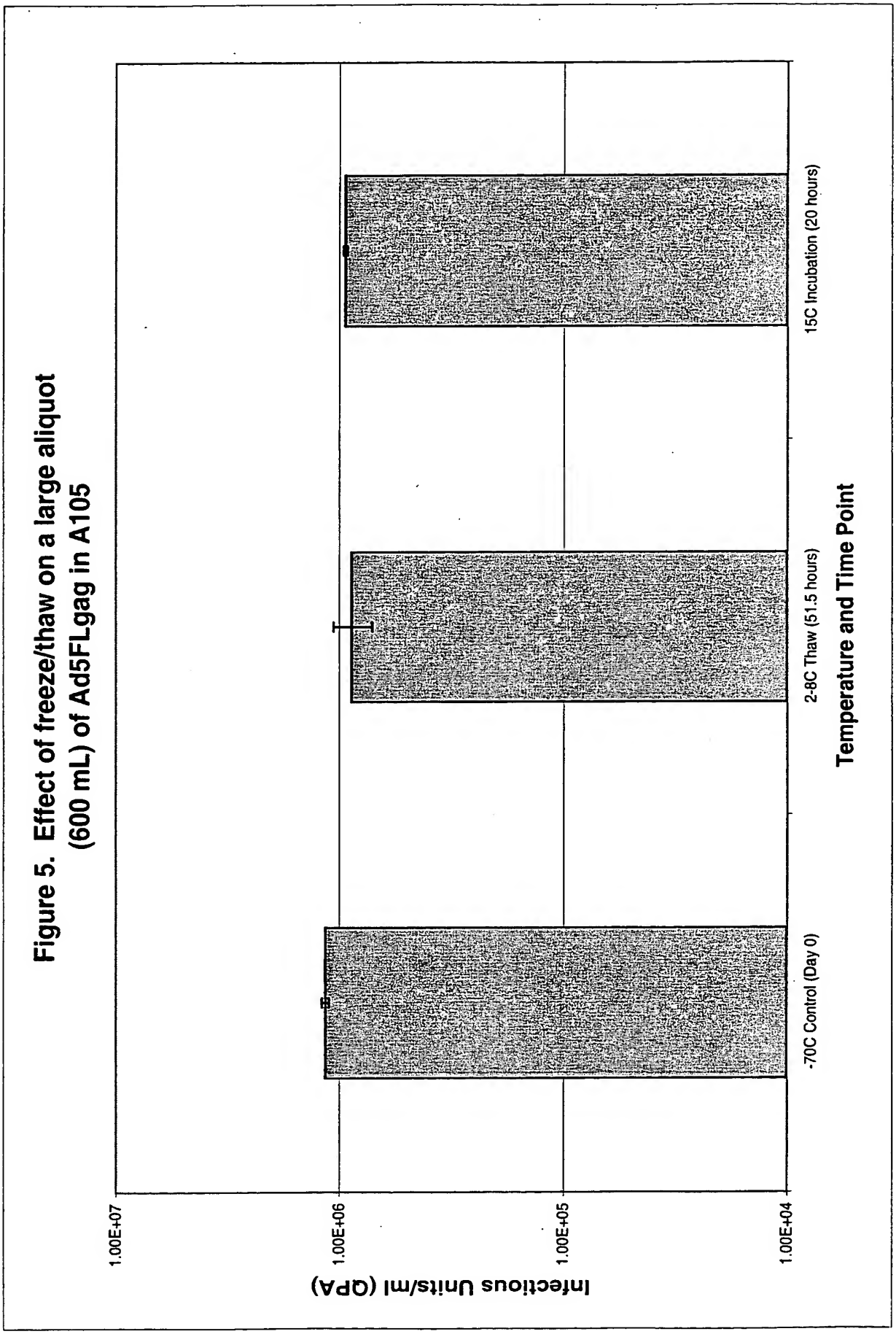


Figure 5. Effect of freeze/thaw on a large aliquot (600 mL) of Ad5FLgag in A105

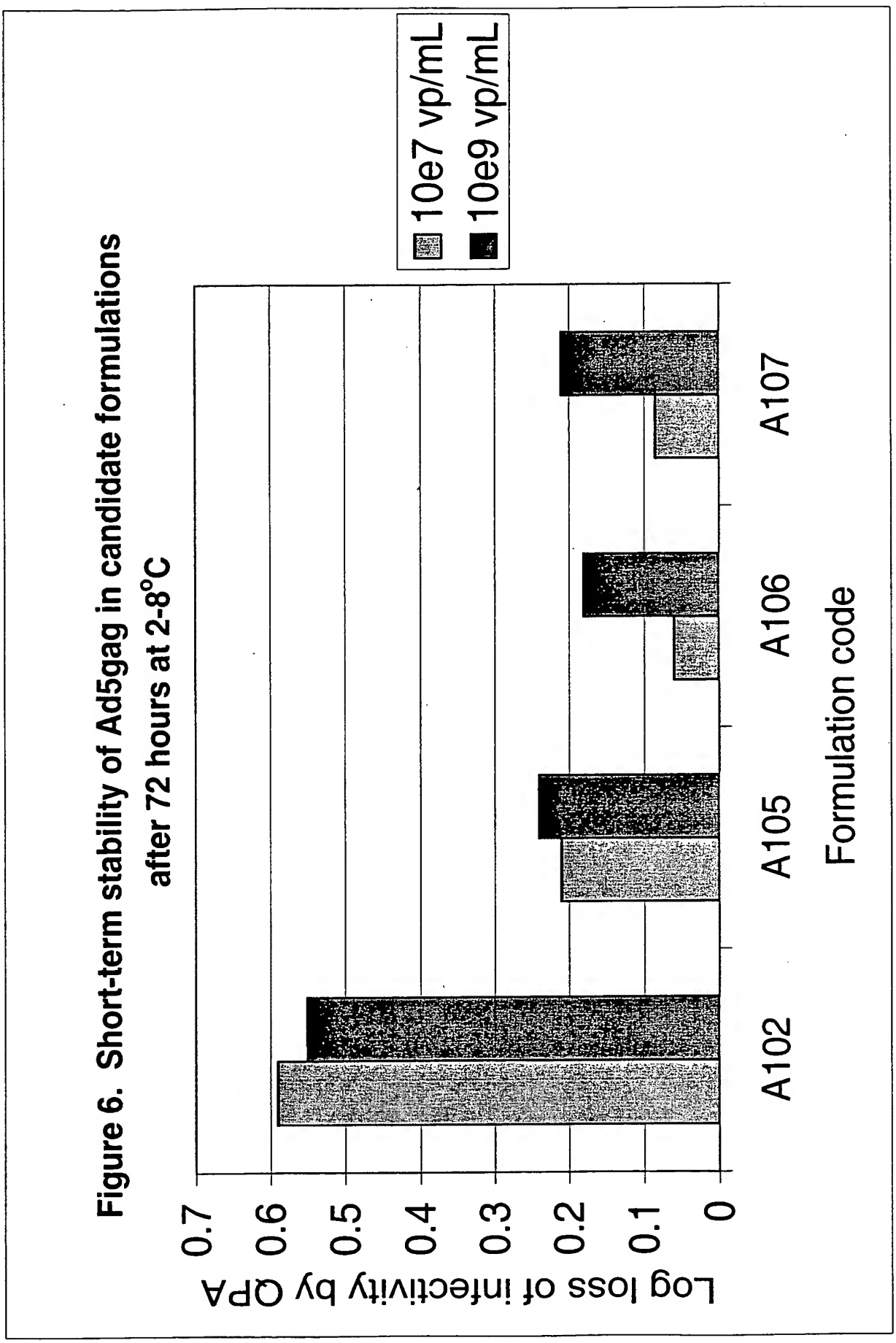


Figure 6. Short-term stability of Ad5gag in candidate formulations after 72 hours at 2-8°C

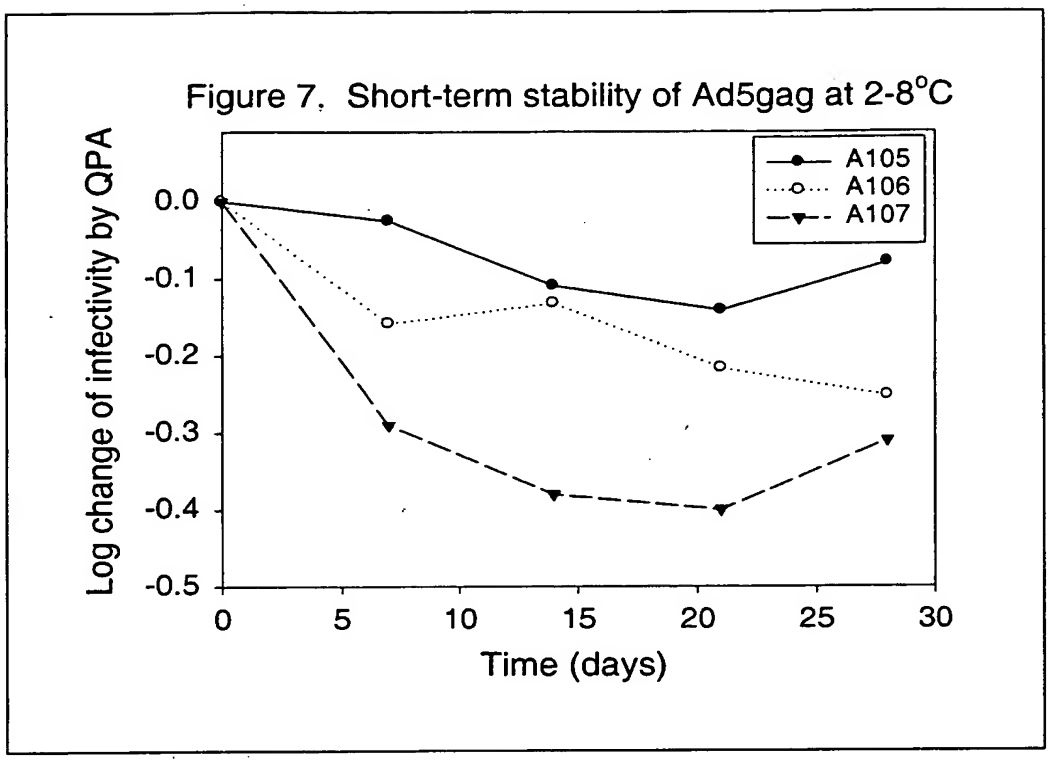


Figure 7. Short-term stability of Ad5gag at 2-8°C
Log change of infectivity by QPA
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
0
5
10
15
20
25
30
Time (days)
A105
A106
A107

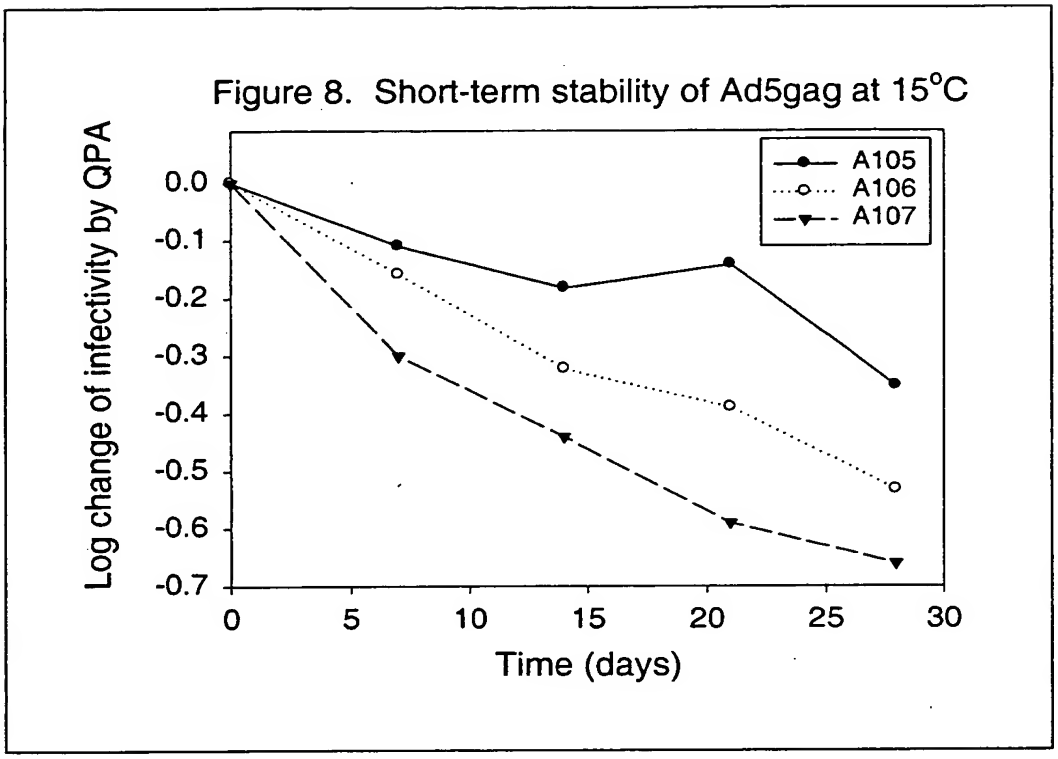


Figure 8. Short-term stability of Ad5gag at 15°C
Log change of infectivity by QPA
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
0
5
10
15
20
25
30
Time (days)
A105
A106
A107

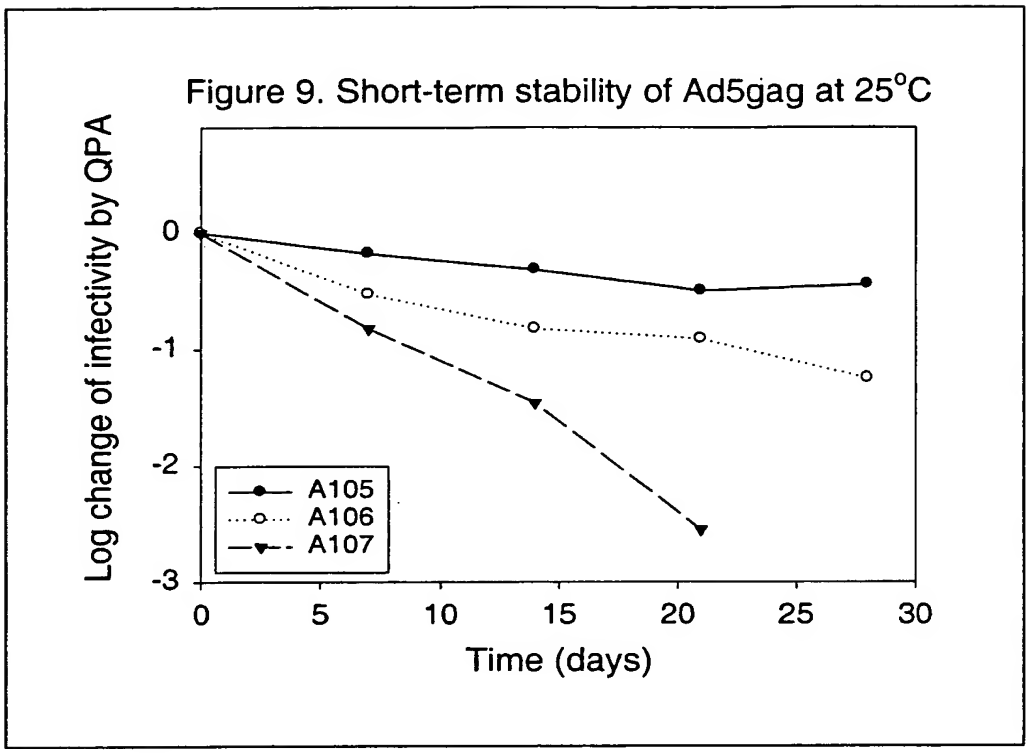


Figure 9. Short-term stability of Ad5gag at 25°C
Log change of infectivity by QPA
0
-1
-2
-3
0
5
10
15
20
25
30
Time (days)
A105
A106
A107

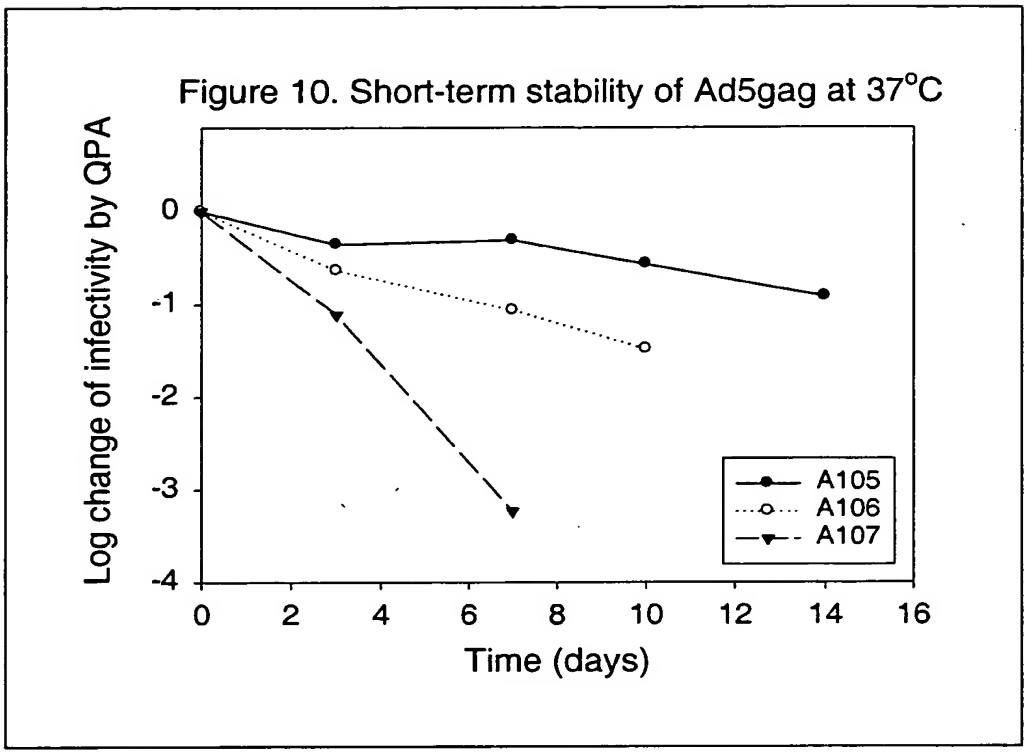


Figure 10. Short-term stability of Ad5gag at 37°C
Log change of infectivity by QPA
0
-1
-2
-3
-4
0
2
4
6
8
10
12
14
16
Time (days)
A105
A106
A107

Figure 11. Arrhenius plot of Ad5gag inactivation at pH 7.4 and pH 8.6

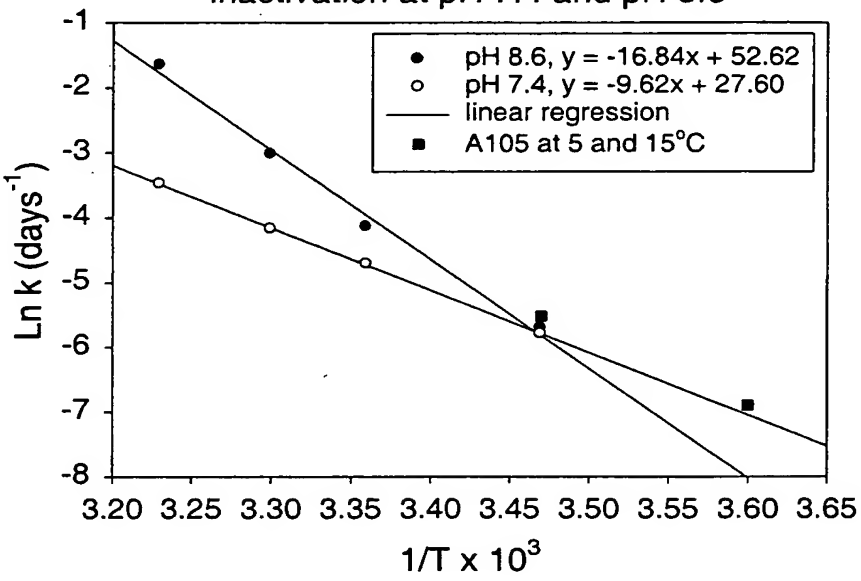
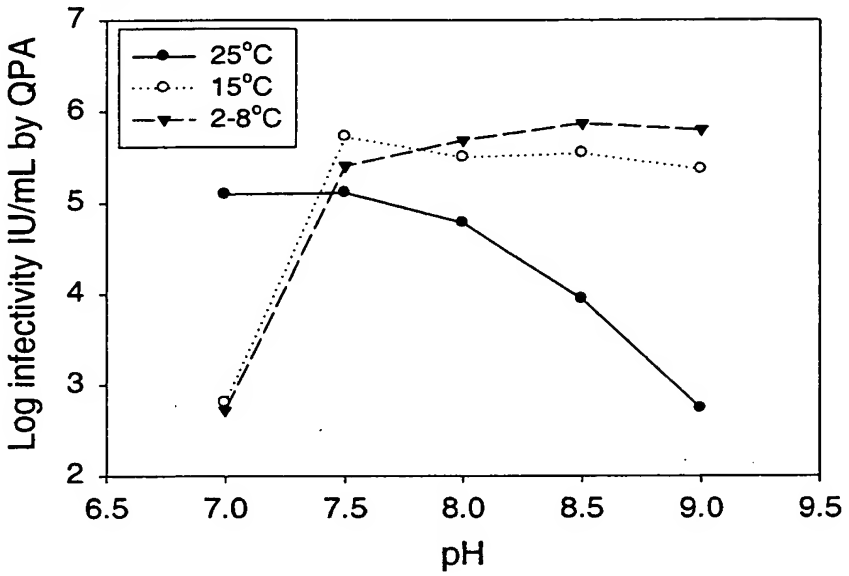


Figure 12. Effect of pH on the stability of Ad5gag



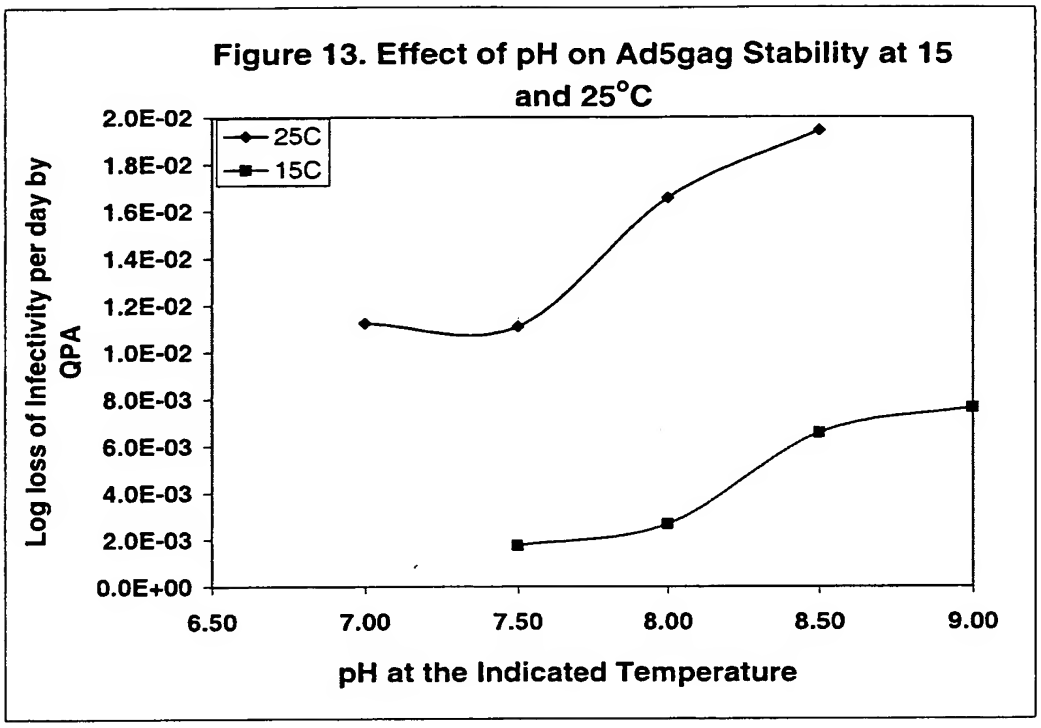


Figure 13. Effect of pH on Ad5gag Stability at 15 and 25°C
Log loss of Infectivity per day by QPA
2.0E-02
1.8E-02
1.6E-02
1.4E-02
1.2E-02
1.0E-02
8.0E-03
6.0E-03
4.0E-03
2.0E-03
0.0E+00
25C
15C
6.50
7.00
7.50
8.00
8.50
9.00
pH at the Indicated Temperature

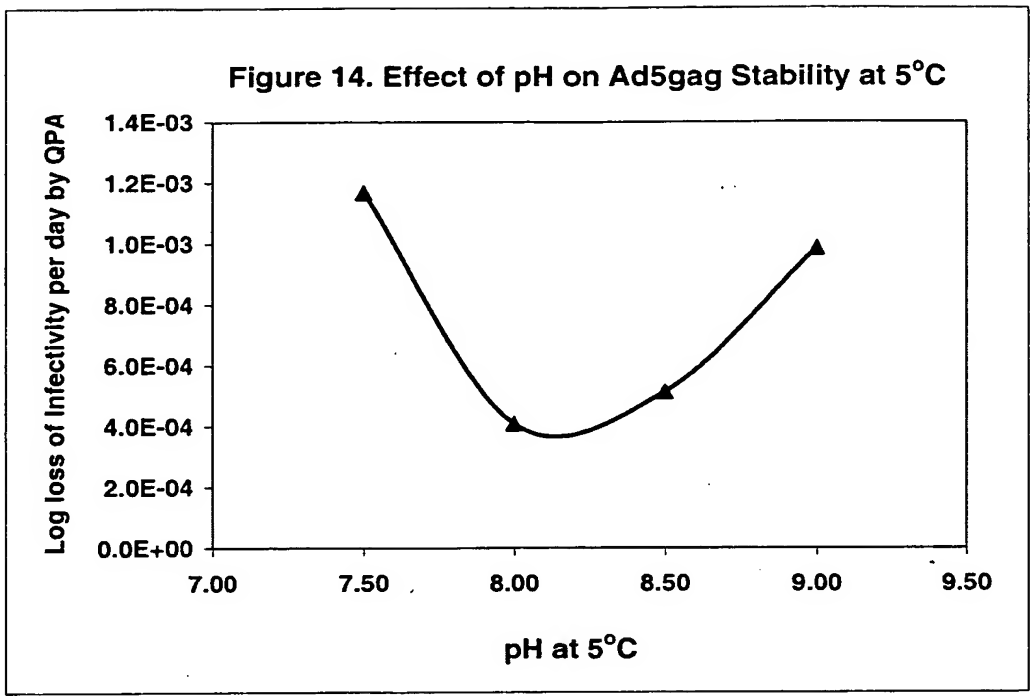
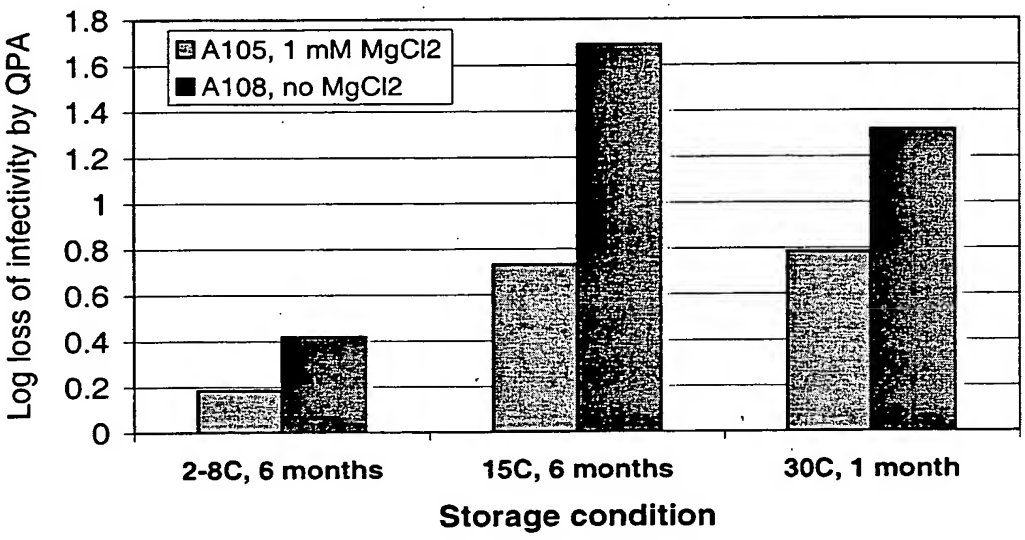


Figure 14. Effect of pH on Ad5gag Stability at 5°C
Log loss of Infectivity per day by QPA
1.4E-03
1.2E-03
1.0E-03
8.0E-04
6.0E-04
4.0E-04
2.0E-04
0.0E+00
7.00
7.50
8.00
8.50
9.00
9.50
pH at 5°C

Figure 15. Effect of $MgCl_2$ on the stability of Ad5gag



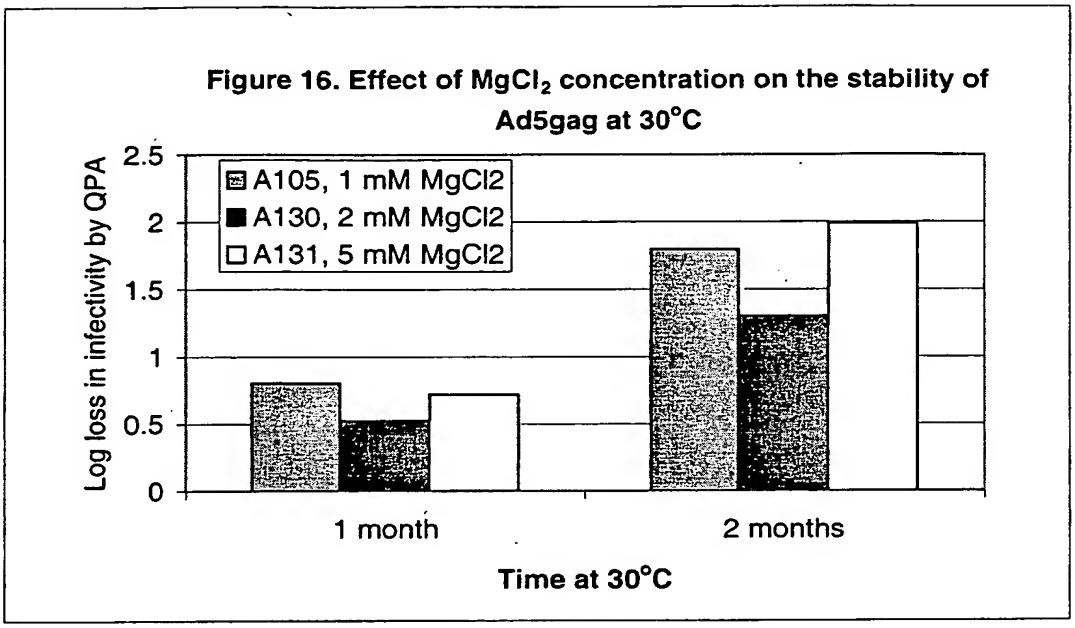


Figure 16. Effect of MgCl2 concentration on the stability of Ad5gag at 30°C
Log loss in infectivity by QPA
2.5
2
1.5
1
0.5
0
A105, 1 mM MgCl2
A130, 2 mM MgCl2
A131, 5 mM MgCl2
1 month
2 months
Time at 30°C

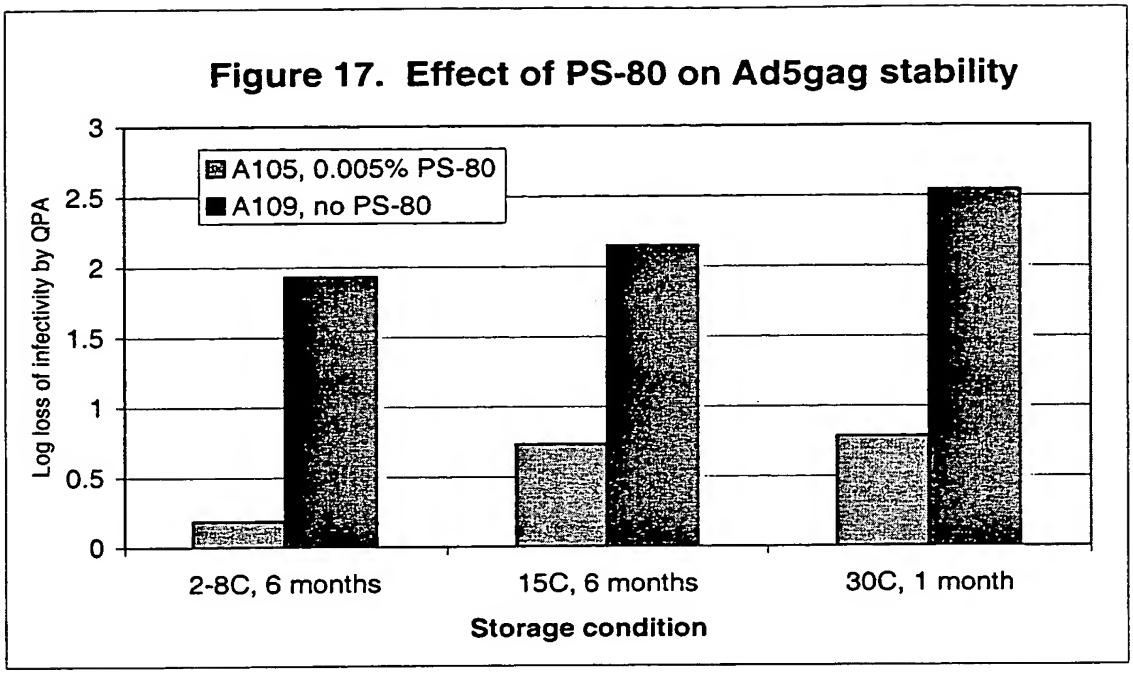


Figure 17. Effect of PS-80 on Ad5gag stability
A105, 0.005% PS-80
A109, no PS-80
Log loss of infectivity by QPA
3
2.5
2
1.5
1
0.5
0
2-8C, 6 months
15C, 6 months
30C, 1 month
Storage condition

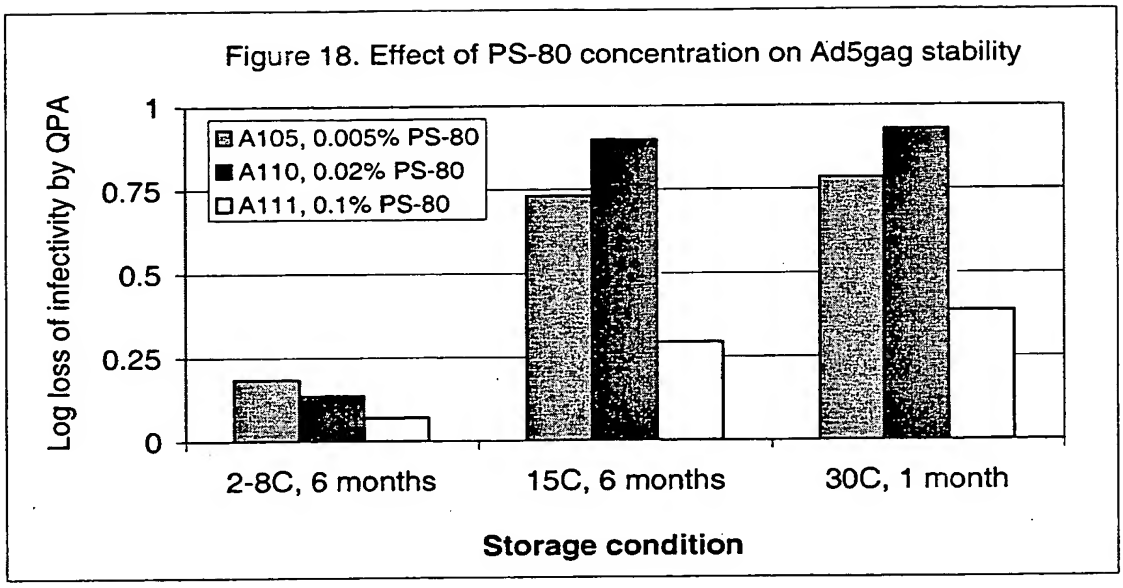
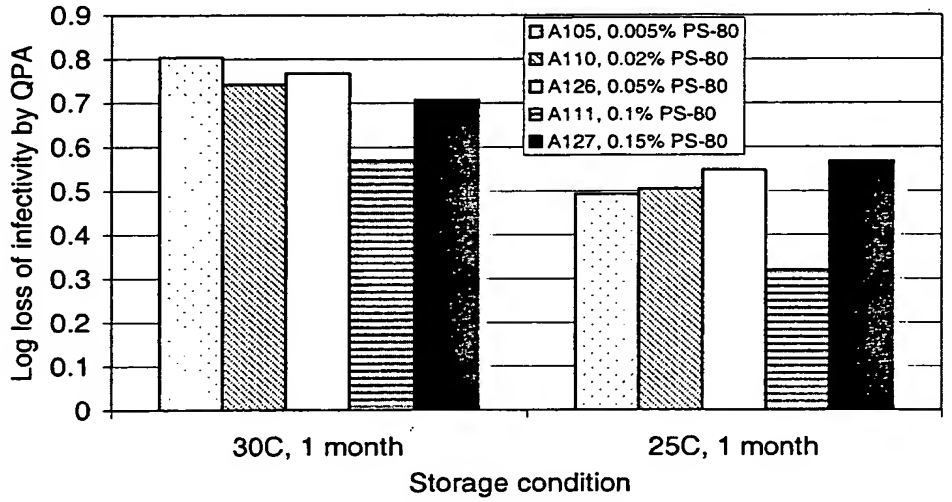


Figure 18. Effect of PS-80 concentration on Ad5gag stability
Log loss of infectivity by QPA
1
0.75
0.5
0.25
0
A105, 0.005% PS-80
A110, 0.02% PS-80
A111, 0.1% PS-80
2-8C, 6 months
15C, 6 months
30C, 1 month
Storage condition

Figure 19. Effect of PS-80 concentration on Ad5gag stability



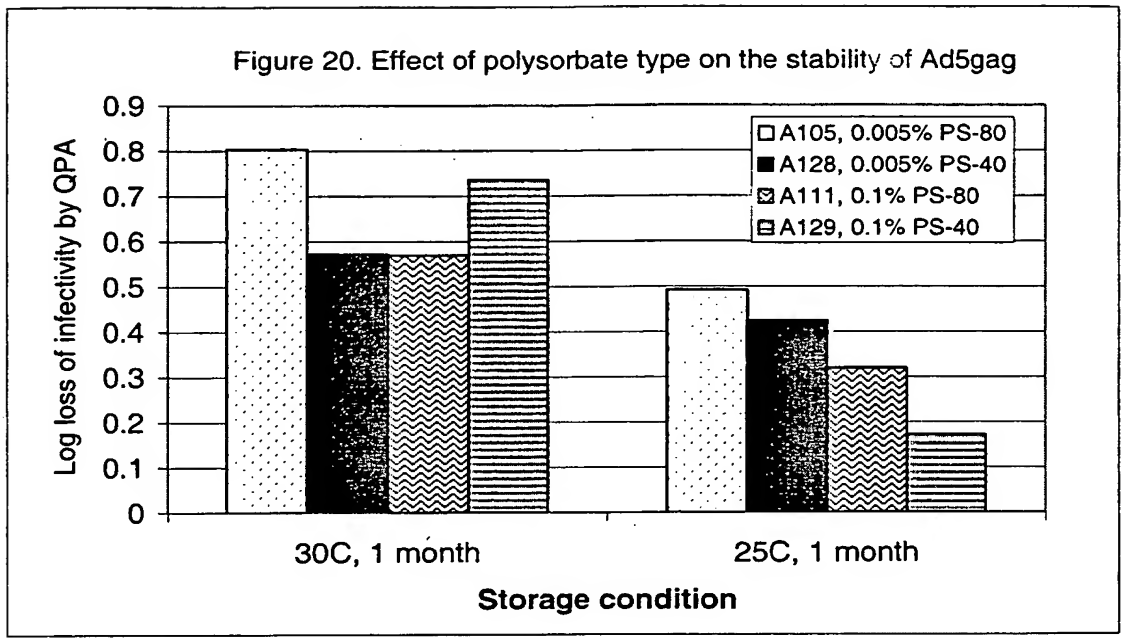
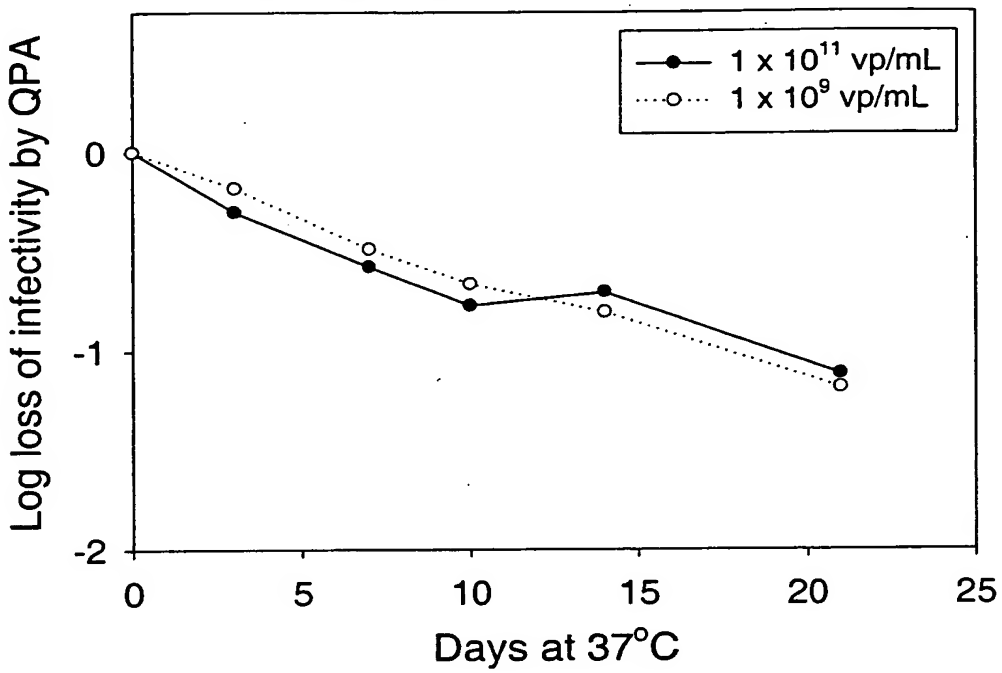


Figure 20. Effect of polysorbate type on the stability of Ad5gag
Log loss of infectivity by QPA
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
A105, 0.005% PS-80
A128, 0.005% PS-40
A111, 0.1% PS-80
A129, 0.1% PS-40
30C, 1 month
25C, 1 month
Storage condition

Figure 21. Effect of Ad5FLgag concentration on storage stability at 37°C in A105



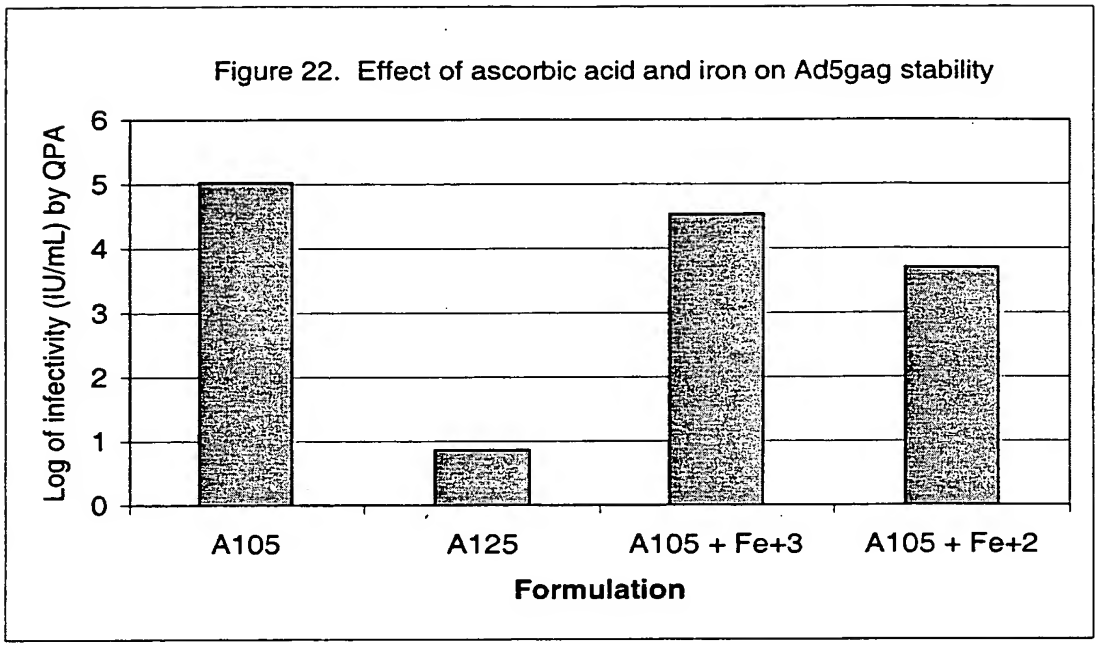
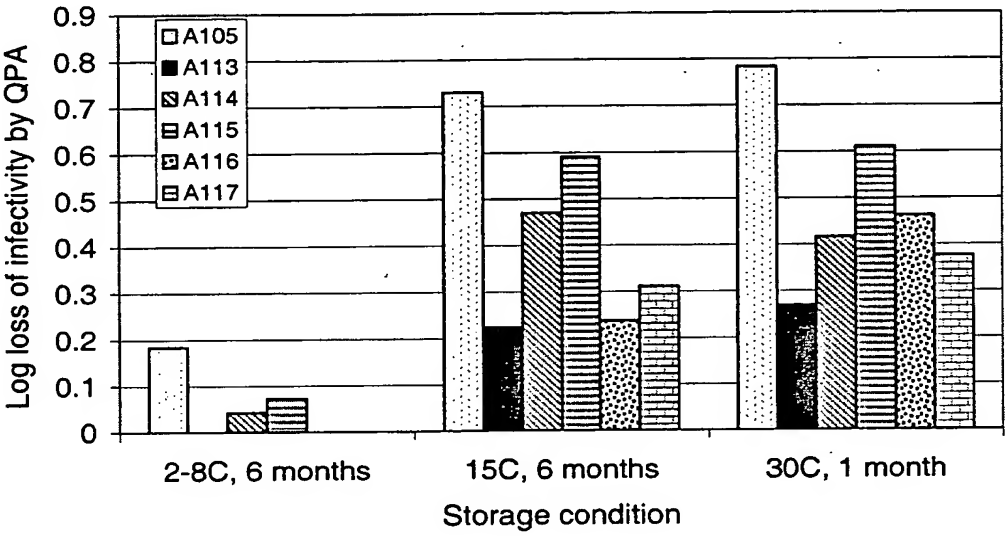


Figure 22. Effect of ascorbic acid and iron on Ad5gag stability
Log of infectivity (IU/mL) by QPA
0
1
2
3
4
5
6
A105
A125
A105 + Fe+3
A105 + Fe+2
Formulation

Figure 23. Effect of oxidation inhibitors on Ad5gag stability



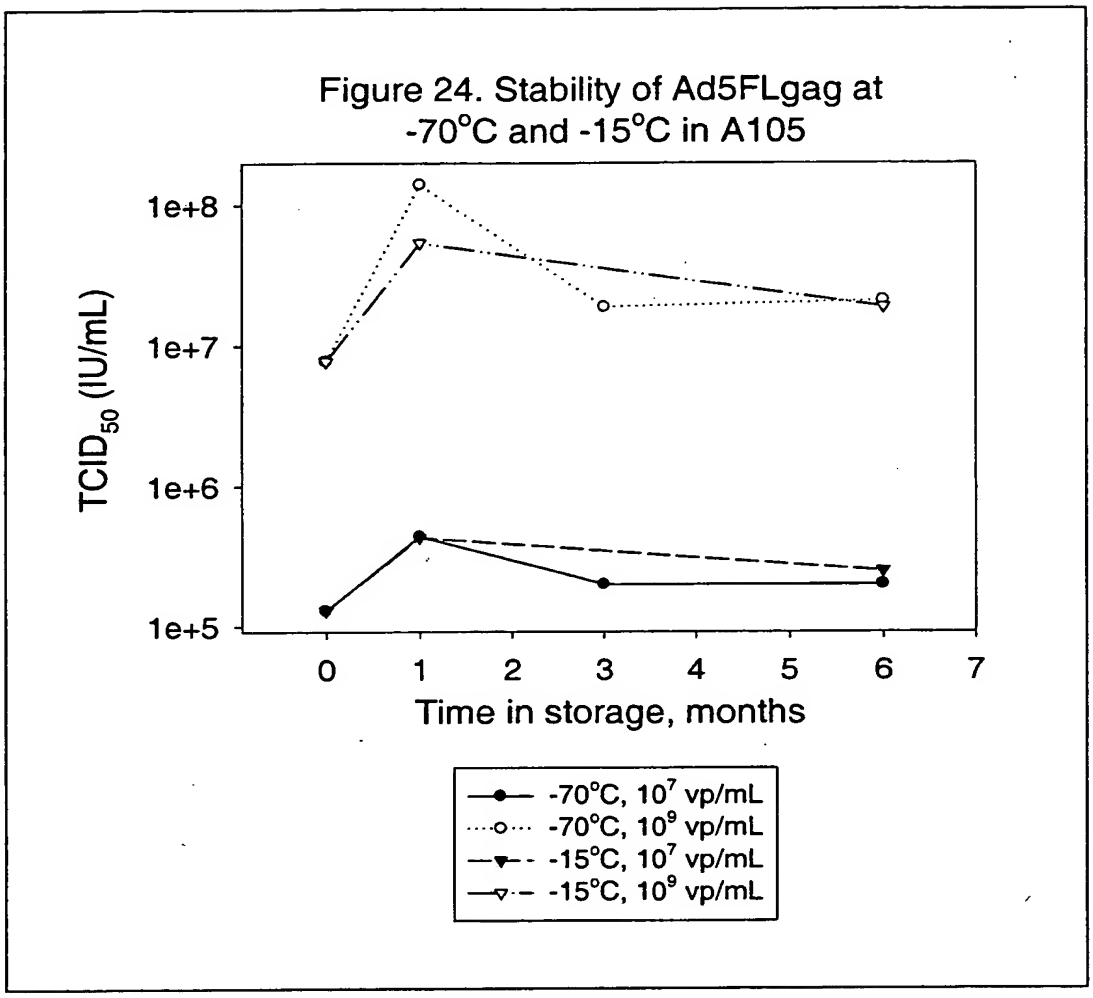


Figure 24. Stability of Ad5FLgag at -70°C and -15°C in A105
TCID50 (IU/mL)
1e+8
1e+7
1e+6
1e+5
0
1
2
3
4
5
6
7
Time in storage, months
-70°C, 10^7 vp/mL
-70°C, 10^9 vp/mL
-15°C, 10^7 vp/mL
-15°C, 10^9 vp/mL

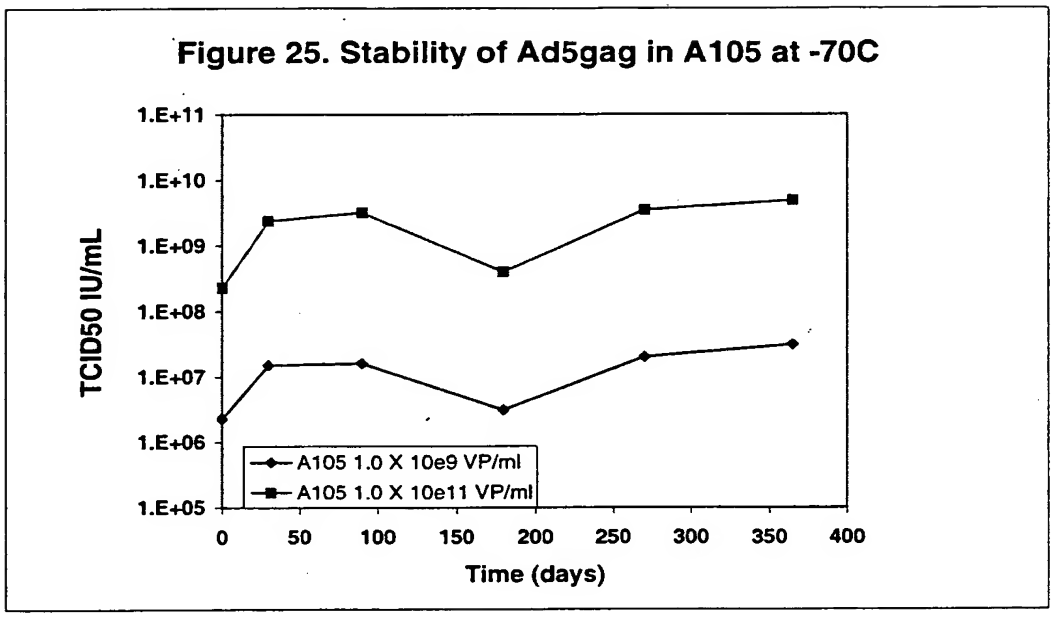


Figure 25. Stability of Ad5gag in A105 at -70C
TCID50 IU/mL
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
0
50
100
150
200
250
300
350
400
Time (days)
A105 1.0 X 10e9 VP/ml
A105 1.0 X 10e11 VP/ml

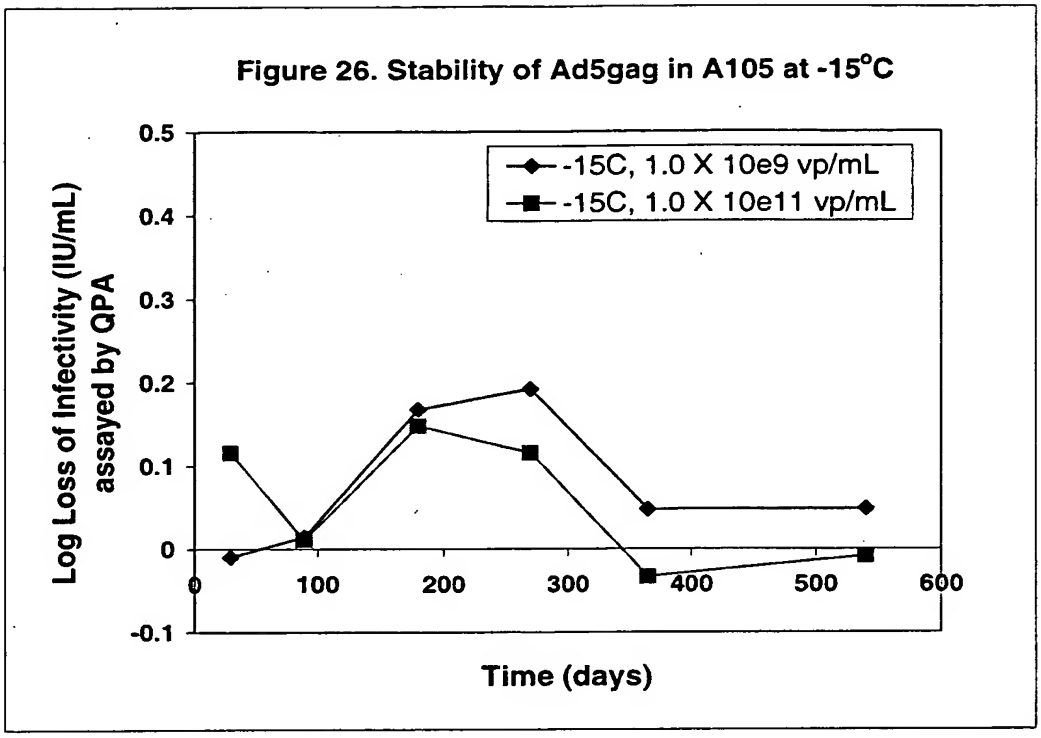


Figure 26. Stability of Ad5gag in A105 at -15°C
Log Loss of Infectivity (IU/mL) assayed by QPA
0.5
0.4
0.3
0.2
0.1
0
-0.1
0
100
200
300
400
500
600
Time (days)
-15C, 1.0 X 10e9 vp/mL
-15C, 1.0 X 10e11 vp/mL

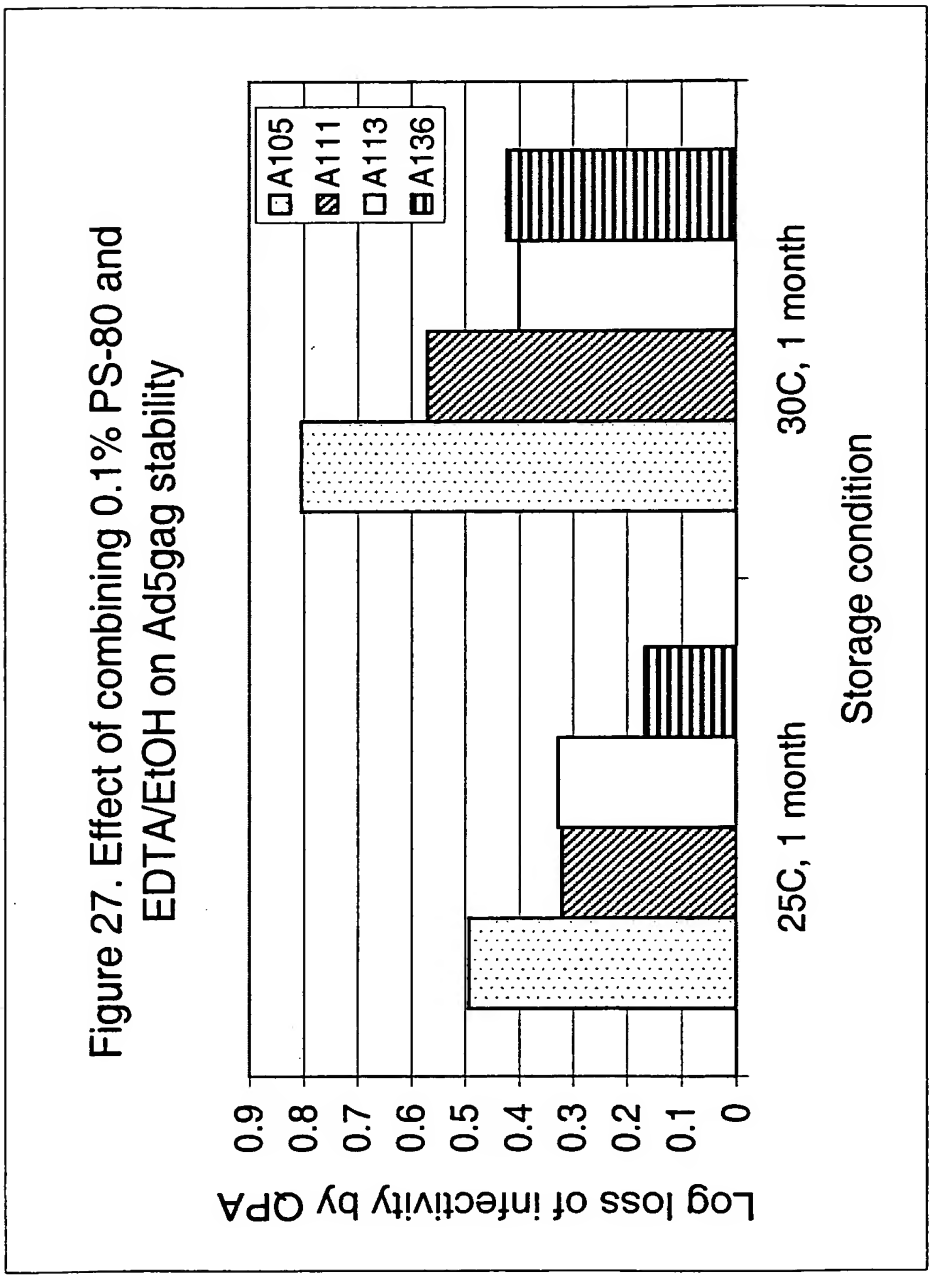


Figure 27. Effect of combining 0.1% PS-80 and EDTA/EtOH on Ad5gag stability

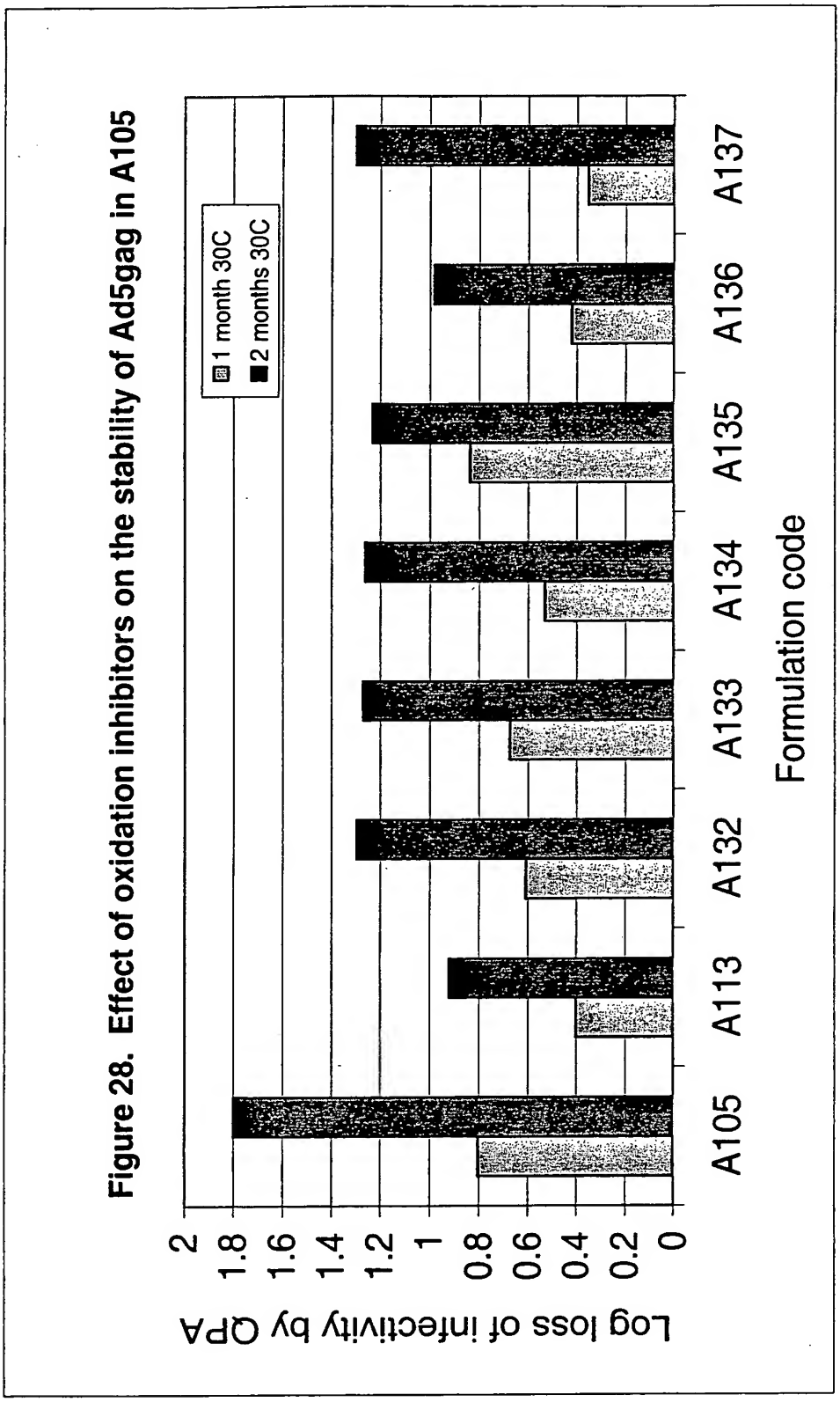


Figure 28. Effect of oxidation inhibitors on the stability of Ad5gag in A105
Log loss of infectivity by QPA
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1 month 30C
2 months 30C
A105
A113
A132
A133
A134
A135
A136
A137
Formulation code

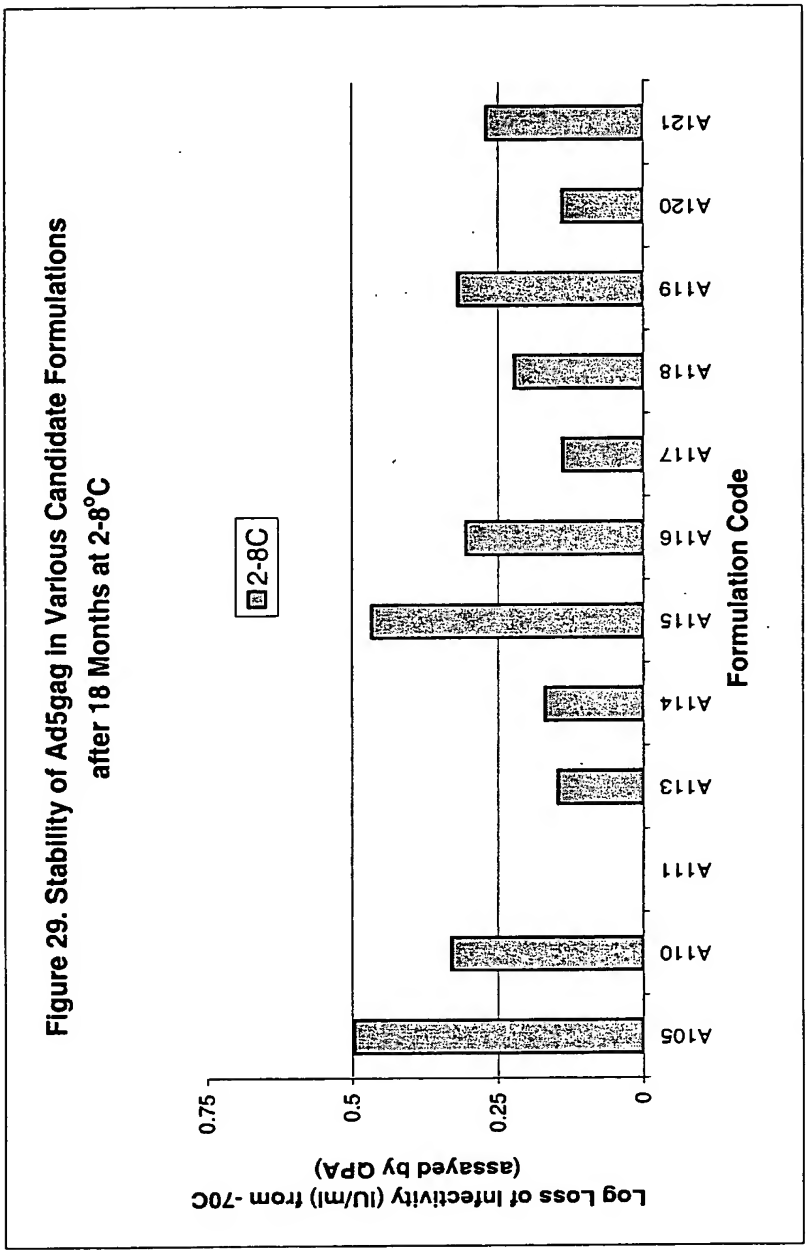


Figure 29. Stability of Ad5gag In Various Candidate Formulations after 18 Months at 2-8°C
2-8C
Log Loss of Infectivity (IU/ml) from -70C (assayed by QPA)
0
0.25
0.5
0.75
A105
A110
A111
A113
A114
A115
A116
A117
A118
A119
A120
A121
Formulation Code

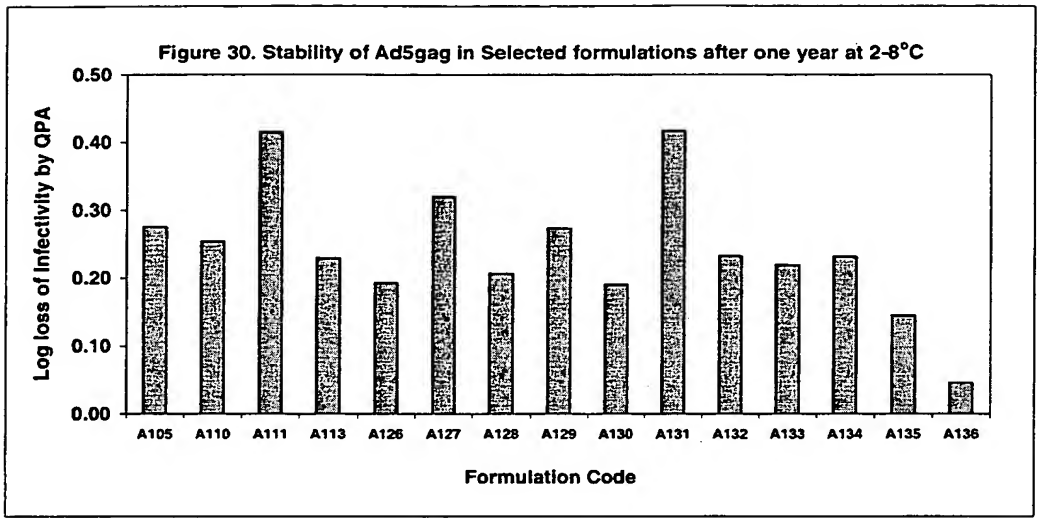


Figure 30. Stability of Ad5gag in Selected formulations after one year at 2-8°C
Log loss of infectivity by QPA
0.50
0.40
0.30
0.20
0.10
0.00
A105
A110
A111
A113
A126
A127
A128
A129
A130
A131
A132
A133
A134
A135
A136
Formulation Code

Figure 31. Stability of Ad5gag in Selected Formulations after 9 months of Storage at 2-8°C and 15°C

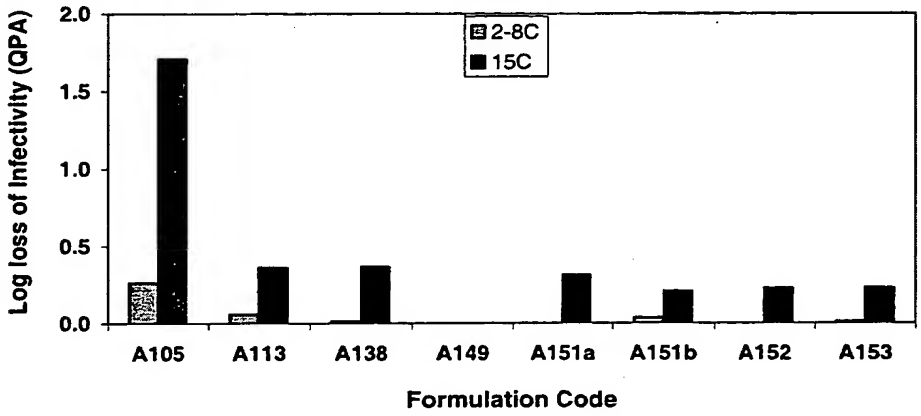


Figure 32. Stability of Ad5gag Candidate Formulations after 9 months of storage at 2-8°C and 15°C